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(54) Title: PROCESSES FOR THE PREPARATION OF 8-CHLORO-1-METHYL-2,3,4,5-TETRAHYDRO-1H-3-BENZAZEPINE AND INTERMEDIATES RELATED THERETO

(57) Abstract: The present invention provides processes, methods and intermediates for the preparation of 8-chloro-1-methyl-2,3,4,5-tetrahydro-1H-3-benzazepine, salts, hydrates and crystal forms thereof which are useful as serotonin (5-HT) receptor agonists for the treatment of, for example, central nervous system disorders such as obesity.



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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2007/008170

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D223/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2005/019179 A (ARENA PHARM INC [US]; BURBAUM BEVERLY W [US]; GILSON CHARLES A III [US] 3 March 2005 (2005-03-03) claims 1,290; examples 6,12	1-21
X	SMITH B M ET AL: "Discovery and SAR of new benzazepines as potent and selective 5-HT _{2C} receptor agonists for the treatment of obesity" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 15, no. 5, 1 March 2005 (2005-03-01), pages 1467-1470, XP004750690 ISSN: 0960-894X page 1468, column 2, line 15 - line 18; table 4; compounds R-15,S-15 ----- -/--	22-27



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

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- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International application No
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2005/003096 A (ARENA PHARM INC [US]; SMITH BRIAN [US]; GILSON CHARLES III [US]; SCHUL) 13 January 2005 (2005-01-13) page 53; example 3.7(step4) -----	22,27
P,X	WO 2006/069363 A (ARENA PHARM INC [US]; AGARWAL RAJESH KUMAR [US]; BETTS III WILLIAM L []) 29 June 2006 (2006-06-29) cited in the application example 2 -----	23

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/008170

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-21

a method for preparing a compound of Formula (I)

2. claim: 22

a method for resolving a mixture of compounds of Formula (Ia) and (Ib)

3. claims: 23-27

a method for preparing a compound of Formula (II)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2007/008170

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005019179 A	03-03-2005	AU 2004267016 A1	03-03-2005
		BR PI0411613 A	08-08-2006
		CA 2529401 A1	03-03-2005
		EP 1636191 A2	22-03-2006
		JP 2007521269 T	02-08-2007
		KR 20060023163 A	13-03-2006
		MX PA05013364 A	17-03-2006
		US 2008045502 A1	21-02-2008
WO 2005003096 A	13-01-2005	AU 2004253888 A1	13-01-2005
		BR PI0411470 A	11-07-2006
		CA 2529320 A1	13-01-2005
		CN 1805938 A	19-07-2006
		CN 1805939 A	19-07-2006
		EP 1633720 A1	15-03-2006
		JP 2007516941 T	28-06-2007
		KR 20060023156 A	13-03-2006
		MX PA05013366 A	05-04-2006
		US 2007142357 A1	21-06-2007
WO 2006069363 A	29-06-2006	AU 2005318959 A1	29-06-2006
		CA 2589988 A1	29-06-2006
		CN 101084193 A	05-12-2007
		EP 1838677 A2	03-10-2007
		KR 20070098870 A	05-10-2007